WEST

Help | Logout

Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers

Generate Collection

Search Results - Record(s) 1 through 3 of 3 returned.

☐ 1. Document ID: US 6033907 A
Entry 1 of 3 File: USPT Mar 7, 2000

US-PAT-NO: 6033907
DOCUMENT-IDENTIFIER: US 6033907 A
TITLE: Enhanced virus-mediated DNA transfer

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 2. Document ID: US 5639759 A
Entry 2 of 3 File: USPT Jun 17, 1997

US-PAT-NO: 5639759
DOCUMENT-IDENTIFIER: US 5639759 A
TITLE: Carbocyclic and heterocyclic fused-ring quinolinecarboxylic acids useful as immunosuppressive agents

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 3. Document ID: US 5428040 A
Entry 3 of 3 File: USPT Jun 27, 1995

US-PAT-NO: 5428040
DOCUMENT-IDENTIFIER: US 5428040 A
TITLE: Carbocyclic fused-ring quinolinecarboxylic acids useful as immunosuppressive agents

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

Generate Collection

```
? s retro(w)nectin

          13486  RETRO
             51  NECTIN
     S1       0  RETRO(W)NECTIN
? s retronectin

     S2       5  RETRONECTIN
? rd

...completed examining records
     S3       3  RD (unique items)
? t s3/3,ab/all


 3/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.

10143610   99374580
  Optimization of retroviral gene transduction of mobilized primitive
hematopoietic progenitors by using thrombopoietin, Flt3, and Kit ligands
and RetroNectin culture.
  Murray L; Luens K; Tushinski R; Jin L; Burton M; Chen J; Forestell S;
Hill B
  SyStemix, a Novartis Company, Palo Alto, CA 94304, USA.
lesley.murray@pharma.novartis.com
  Hum Gene Ther (UNITED STATES) Jul 20 1999, 10 (11) p1743-52, ISSN
1043-0342 Journal Code: A12
  Languages: ENGLISH
  Document type: JOURNAL ARTICLE
  We have investigated the ability of several cytokine combinations to
improve retrovirus-mediated transduction of human primitive hematopoietic
progenitors (PHPs) from mobilized peripheral blood (MPB). Retroviral
infection of CD34+ cells was performed by culture on fibronectin fragment
CH-296 (RetroNectin , RN), using the truncated human nerve growth
factor receptor (NGFR) as the transgene reporter. Transgene expression
among progeny of PHPs was assayed by FACS analysis after long-term stromal
culture (LTC). Transgene delivery to PHPs was assessed by PCR of individual
stromal culture-derived methylcellulose colonies (LTC-CFCs). Compared with
interleukin 3 (IL-3), IL-6, and leukemia inhibitory factor (LIF), the
combination of thrombopoietin (TPO), Flt3 ligand (FL), and Kit ligand (KL)
effected a 73-fold increase in NGFR expression among CD34+ cells (to 14%)
and a 14-fold increase in NGFR expression among total cells (to 10%) after
LTC. In addition, a 2.4-fold increase in neo gene marking of LTC-CFCs was
observed. A preclinical study comparing the effect of high-speed
centrifugation ("spinoculation") or culture on RN during exposure to
retroviral particles in teflon cell culture bags showed no difference in
the efficiency of transduction of PHPs between these two methods.


 3/3,AB/2     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2000 BIOSIS. All rts. reserv.

12288779   BIOSIS NO.: 200000046646
Immobilization of suspension cells on extracellular matrix: An on and off
  affair.
AUTHOR: Prokopishyn Nicole L(a); Barron Gina L(a); Carsrud N D Victor(a);
```

Brown David B(a); Yannariello-Brown Judith(a)
AUTHOR ADDRESS: (a)Gene-Cell, Inc., Houston, TX**USA
JOURNAL: Blood 94 (10 SUPPL. 1 PART 2):p167b Nov. 15, 19
CONFERENCE/MEETING: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999
SPONSOR: The American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

3/3,AB/3 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11867777 BIOSIS NO.: 199900113886
Transduction kinetics of non-human primate immuno-selected CD34+ cells using retroviral and lentiviral vectors that express the green fluorescent protein.
AUTHOR: Donahue R E(a); Rowe T K; Sorrentino B P; Hawley R G; An D S; Chen I S Y; Wersto R P
AUTHOR ADDRESS: (a)Hematol. Branch, NHLBI, Rockville, MD**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p376B Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

```
    ---  -----  -----------
? s ch(w)296

          383776  CH
            5458  296
      S1      46  CH(W)296
? rd

...completed examining records
      S2      30  RD (unique items)
? t s2/3,ab/all


 2/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.

10254003   20094665
  High levels of lymphoid expression of enhanced green fluorescent protein
in nonhuman primates transplanted with cytokine-mobilized peripheral blood
CD34(+) cells.
  Donahue RE; Wersto RP; Allay JA; Agricola BA; Metzger ME; Nienhuis AW;
Persons DA; Sorrentino BP
  Hematology Branch, National Heart, Lung, and Blood Institute, Rockville,
MD 20550, USA.
  Blood (UNITED STATES)  Jan 15 2000,  95 (2) p445-52,  ISSN 0006-4971
Journal Code: A8G
  Contract/Grant No.: P01HL53749, HL, NHLBI
  Languages: ENGLISH
  Document type: JOURNAL ARTICLE
  We have used a murine retrovirus vector containing an enhanced green
fluorescent protein complimentary DNA (EGFP cDNA) to dynamically follow
vector-expressing cells in the peripheral blood (PB) of transplanted rhesus
macaques. Cytokine mobilized CD34(+) cells were transduced with an
amphotropic vector that expressed EGFP and a dihydrofolate reductase cDNA
under control of the murine stem cell virus promoter. The transduction
protocol used the CH-296 recombinant human fibronectin fragment
and relatively high concentrations of the flt-3 ligand and stem cell
factor. Following transplantation of the transduced cells, up to 55%
EGFP-expressing granulocytes were obtained in the peripheral circulation
during the early posttransplant period. This level of myeloid marking,
however, decreased to 0.1% or lower within 2 weeks. In contrast, EGFP
expression in PB lymphocytes rose from 2%-5% shortly following
transplantation to 10% or greater by week 5. After 10 weeks, the level of
expression in PB lymphocytes continued to remain at 3%-5% as measured by
both flow cytometry and Southern blot analysis, and EGFP expression was
observed in CD4(+), CD8(+), CD20(+), and CD16/56(+) lymphocyte subsets.
EGFP expression was only transiently detected in red blood cells and
platelets soon after transplantation. Such sustained levels of lymphocyte
marking may be therapeutic in a number of human gene therapy applications
that require targeting of the lymphoid compartment. The transient
appearance of EGFP(+) myeloid cells suggests that transduction of a
lineage-restricted myeloid progenitor capable of short-term engraftment was
obtained with this protocol. (Blood. 2000;95:445-452)


 2/3,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
```

10222167 20051163
Enhanced retroviral gene transfer into CML and normal bone marrow, and CML and mobilized peripheral blood CD34+ cells using the recombinant fibronectin fragment **CH-296**.
Garrett E; Garin MI; Miller AR; Goldman JM; Melo JV; Apperley JF
Department of Haematology, Imperial College School of Medicine, Hammersmith Hospital, London.
Br J Haematol (ENGLAND) Nov 1999, 107 (2) p401-8, ISSN 0007-1048 Journal Code: AXC
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Autologous stem cell transplantation is a therapeutic alternative for many chronic myeloid leukaemia (CML) patients ineligible for the only curative treatment of allogeneic bone marrow transplantation. In this study the retroviral transduction of CD34+ progenitor cells isolated from the bone marrow (BM) and peripheral blood (PB) of patients with CML was compared to that of CD34+ cells isolated from the BM and PB of normal individuals and patients with non-haematological malignancies. A highly significant increase in transduction of all cell types was achieved in the presence of the recombinant fibronectin fragment, **CH-296** ($P < 0.05$). In the absence of fibronectin, centrifugation produced a marginal improvement in the transduction of all cell types, which was significant only for CMLBM progenitor cells ($P < 0.05$). There was no significant additive effect when centrifugation was included in the fibronectin infection protocol. In the presence of **CH-296**, combinations of three or more cytokines improved transduction for all cell types. The same degree of transduction was observed for both normal and CML cells, irrespective of the variations employed in the infection protocol, suggesting that both leukaemic and non-leukaemic progenitors are equally susceptible to retroviral infection. These results demonstrate that **CH-296** has a universal beneficial effect on the transduction of haemopoietic progenitor cells, with clear potential for future clinical trials.

2/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10184542 20049626
Increased gene transfer into human cord blood cells by centrifugation-enhanced transduction in fibronectin fragment-coated tubes.
Sanyal A; Schuening FG
Bone Marrow Transplant Division, University of Wisconsin, Madison 53792, USA.
Hum Gene Ther (UNITED STATES) Nov 20 1999, 10 (17) p2859-68, ISSN 1043-0342 Journal Code: A12
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We investigated whether transduction of human cord blood progenitor cells can be increased by spinoculation in fibronectin fragment **CH-296** (FN)-coated tubes. Bicistronic vectors PA317/LgEIN, containing the enhanced green fluorescent protein (EGFP) and neomycin phosphotransferase (neo) genes, and PG13/LgDIN, containing the dihydrofolate reductase and neo genes, were used to transduce CD34-enriched human cord blood cells. Transduction by spinoculation in FN-coated tubes (spin/FN+) was compared with spinoculation in noncoated tubes (spin/FN-) and transduction in plates coated with FN (plate/FN+). Antibody to TGF-beta was added to spin/FN+ to evaluate its impact on transduction. Using producer cell line PA317/LgEIN for transduction of CD34+ cord blood cells, FACS analysis for expression of EGFP revealed mean transduction of 30.6+/-4.3, 9.1+/-1.6, and 21.1+/-6.5% of CD34+ cells in the spin/FN+, spin/FN-, and plate/FN+ arms, respectively. Transduction of CD+CD38low cells was also higher in the spin/FN+ arm as compared with transduction in

the spin/FN- arm. These results were corroborated by colony-forming assays. Antibody to TGF-beta did not further increase transduction. Using a different producer cell line, PG13/pLgDIN, a higher number of G418-resistant CFU-GM was observed in the spin/FN+ as compared with the plate/FN+ and spin/FN-arms. NOD/SCID mice were transplanted with transduced, CD34-enriched human cord blood cells, and persistence of transduced human cells was analyzed in the mice marrows after 6-8 weeks: 32.8, 6.0, and 23.9% human G418-resistant CFU-GM colonies were observed in the spin/FN+, spin/FN-, and plate/FN+ arms, respectively. These results suggest that spinoculation in FN-coated tubes increases transduction of early human cord blood progenitor cells as compared with spinoculation in noncoated tubes.

2/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10149355 99440289

Adenovirus and retrovirus mediated interferon alpha gene transfer into CD34+ cells maintains regeneration capacity and enhances adhesion molecules in K562 cells.

Seiter K; Kancherla R; Yang L; Quan S; Farley TJ; Abraham NG; Ahmed T
Department of Medicine, New York Medical College, Valhalla 10595, USA.

J Investig Med (UNITED STATES) Sep 1999, 47 (8) p414-24, ISSN 1081-5589 Journal Code: B9K
Contract/Grant No.: HL54138, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

BACKGROUND: Systemic administration of interferon-alpha (IFN-alpha) results in cytogenetic remissions and enhanced survival in a significant percentage of patients with chronic mylogenous leukemia (CML) and lymphoma. However, this treatment is associated with deleterious toxic effects. Gene transfer of the IFN-alpha gene into hematopoietic progenitors represents a novel strategy to deliver high concentrations of IFN-alpha to a local area. METHODS: We compared the effect of the transfer of the IFN-alpha gene on the cell growth and differentiation of several CD34+ cells in culture and in a NOD/SCID animal model, using adenovirus and retrovirus constructs. RESULTS: Transient local expression of the IFN-alpha gene using an adenovirus vector was associated with normal proliferation of CD34+ progenitors as measured by a colony forming unit of granulocyte-macrophage (CFU-GM) growth. Flow cytometric determination revealed that there was no significant difference in viability of these cells for 24-hour transduction periods. Reverse transcriptase/polymerase chain reaction (RT-PCR) analysis of RNA from CD34+ harvested CFU-GM progenitors demonstrated expression of IFN-alpha mRNA; radioimmunoassay (RIA) revealed that transduced cells secreted substantial levels of IFN-alpha protein. Furthermore, we constructed a retroviral vector in which IFN-alpha cDNA was driven by a viral LTR promoter to evaluate the effect of permanent IFN-alpha gene expression on cell growth. Retroviral packaging cells PA317 with high titers of retrovirus were produced and used to infect CD34+ and K562 cells. RIA showed that IFN-alpha-transduced CD34+ cells (with the aid of fibronectin fragment **CH-296**) produced approximately 400 units of IFN-alpha protein compared to CD34+ cells, or cells transduced with empty vector. IFN-alpha transduced CD34+ generated similar numbers of CFU-GM colonies as compared to control CD34+ cells. Engraftment of CD34+ cells transduced with IFN-alpha gene in NOD/SCID mice was successful for the first 30 days. Additionally, we studied the effect of local IFN-alpha expression on the cellular adhesion molecules, VLA-4, Mac-1, ICAM-1, and L-selectin in K562 cells, and human umbilical endothelial vein cells. K562 cells transduced with the IFN-alpha gene expressed a significantly elevated level of VLA-4, Mac-1, and ICAM-1. CONCLUSIONS: We conclude that expression of the IFN-alpha gene using retrovirus vectors results in an adequate localized expression of IFN-alpha mRNA and protein.

2/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10144833 99428313
The use of granulocyte colony-stimulating factor during retroviral transduction on fibronectin fragment **CH-296** enhances gene transfer into hematopoietic repopulating cells in dogs.
Goerner M; Bruno B; McSweeney PA; Buron G; Storb R; Kiem HP
Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA.
Blood (UNITED STATES) Oct 1 1999, 94 (7) p2287-92, ISSN 0006-4971
Journal Code: A8G
Contract/Grant No.: HL36444, HL, NHLBI; HL03701, HL, NHLBI; DK42716, DK, NIDDK; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A competitive repopulation assay in the dog was used to develop improved gene transfer protocols for hematopoietic stem cell gene therapy. Using this assay, we previously showed improved gene transfer into canine hematopoietic repopulating cells when CD34-enriched marrow cells were cocultivated on gibbon ape leukemia virus (GALV)-based retrovirus vector-producing cells. In the present study, we have investigated the use of fibronectin fragment **CH-296** and 2 growth factor combinations to further improve gene transfer efficiency. CD34-enriched marrow cells from each dog were prestimulated for 24 hours and then divided into 3 equal fractions. Two fractions were placed into flasks coated with either **CH-296** or bovine serum albumin (BSA) and virus-containing medium supplemented with growth factors, and protamine sulfate was replaced 4 times over a 48-hour period. One fraction was cocultivated on irradiated PG13 (GALV-pseudotype) packaging cells for 48 hours. In 2 animals, cells of the different fractions were transduced in the presence of human FLT-3 ligand (FLT3L), canine stem cell factor (cSCF), and human megakaryocyte growth and development factor (MGDF), and in 2 other dogs, transduction was performed in the presence of FLT3L, cSCF, and canine granulocyte-colony stimulating factor (cG-CSF). The vectors used contained small sequence differences, allowing differentiation of cells genetically marked by the different vectors. After transduction, nonadherent and adherent cells from all 3 fractions were pooled and infused into lethally irradiated dogs. Polymerase chain reaction and Southern blot analysis were used to determine the persistence of the transferred vectors in the peripheral blood and marrow cells after transplantation. The highest levels of gene transfer were obtained when cells were transduced in the presence of FLT3L, cSCF, and cG-CSF (gene transfer levels of more than 10% for more than 8 months so far). Compared with the 2 animals that received cells transduced with FLT3L, cSCF, and MGDF, gene transfer levels were significantly higher when dogs received cells that were transduced in the presence of cG-CSF. Transduction on **CH-296** resulted in gene transfer levels that were at least as high as transduction by cocultivation. In summary, the overall levels of gene transfer obtained with these conditions should be sufficiently high to allow stem cell gene therapy studies aimed at correcting genetic diseases in dogs as a model for human gene therapy.

2/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10143610 99374580
Optimization of retroviral gene transduction of mobilized primitive hematopoietic progenitors by using thrombopoietin, Flt3, and Kit ligands and RetroNectin culture.
Murray L; Luens K; Tushinski R; Jin L; Burton M; Chen J; Forestell S; Hill B

SyStemix, a Novartis Company, Palo Alto, CA 94304, USA. lesley.murray@pharma.novartis.com
Hum Gene Ther (UNITED STATES) Jul 20 1999, 10 (11) p1743-52, ISSN 1043-0342 Journal Code: A12
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have investigated the ability of several cytokine combinations to improve retrovirus-mediated transduction of human primitive hematopoietic progenitors (PHPs) from mobilized peripheral blood (MPB). Retroviral infection of CD34+ cells was performed by culture on fibronectin fragment **CH-296** (RetroNectin, RN), using the truncated human nerve growth factor receptor (NGFR) as the transgene reporter. Transgene expression among progeny of PHPs was assayed by FACS analysis after long-term stromal culture (LTC). Transgene delivery to PHPs was assessed by PCR of individual stromal culture-derived methylcellulose colonies (LTC-CFCs). Compared with interleukin 3 (IL-3), IL-6, and leukemia inhibitory factor (LIF), the combination of thrombopoietin (TPO), Flt3 ligand (FL), and Kit ligand (KL) effected a 73-fold increase in NGFR expression among CD34+ cells (to 14%) and a 14-fold increase in NGFR expression among total cells (to 10%) after LTC. In addition, a 2.4-fold increase in neo gene marking of LTC-CFCs was observed. A preclinical study comparing the effect of high-speed centrifugation ("spinoculation") or culture on RN during exposure to retroviral particles in teflon cell culture bags showed no difference in the efficiency of transduction of PHPs between these two methods.

2/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10060577 99321293

Soluble bone marrow stroma factors improve the efficiency of retroviral transfer of the human multidrug resistance 1 gene to human mobilized peripheral blood progenitor cells.

Schiedlmeier B; Buss EC; Veldwijk MR; Zeller WJ; Fruehauf S
German Cancer Research Center, Research Program Diagnostics and Experimental Therapy, Heidelberg.
Hum Gene Ther (UNITED STATES) Jun 10 1999, 10 (9) p1443-52, ISSN 1043-0342 Journal Code: A12
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Hematopoietic stem cells (HSCs) are a potential target for the retrovirus-mediated transfer of chemotherapeutic drug resistance genes. For integration of the proviral DNA in the HSC genome cell division is required. In the bone marrow (BM) hematopoiesis occurs in the vicinity of stroma cells. Soluble stroma components were shown to play a permissive role for the proliferation of lineage-committed and primitive hematopoietic progenitors in conjunction with cytokines. We investigated the effect of stroma-conditioned medium (SCM) of the FBMD1 cell line on the gene transfer rate of the human multidrug resistance 1 (MDR1) gene contained in the retroviral SF-MDR vector into human mobilized peripheral blood progenitor cells (PBPCs) from tumor patients (n = 14) during transwell transduction in the presence of the recombinant fibronectin fragment **CH-296**.
Addition of SCM during transduction increased the gene transfer efficiency into myeloid lineage-committed colony-forming cells by an average of 1.5-fold ($p = 0.02$) as detected by an SF-MDR provirus-specific polymerase chain reaction (PCR). These data were paralleled by significantly ($p = 0.04$ to $p = 0.007$) higher proportions of MDR1-expressing myelo-monocytic progeny after transduction in SCM plus interleukin 3 (IL-3), IL-3/Flt3 ligand (FL), IL-3/IL-6/FL, or IL-3/IL-6/stem cell factor (SCF) when compared with transductions without SCM as measured by rhodamine-123 exclusion. A similar trend was observed for SCM employed in combination with IL-3/IL-6/SCF/FL or FL/thrombopoietin (TPO)/SCF during transduction. The latter combination plus SCM yielded the highest proportion, 19.16 +/- 3.10% Rh-123dull cells.

The beneficial effect of SCM on transduction efficiency was confirmed in additional four patients' samples, using a serum-free viral supernatant transduction protocol. [redacted] soluble BM stroma factors [redacted] able to increase the efficiency of retrovirus-mediated gene transfer into committed progenitor cells, beyond that achieved with fibronectin fragment **CH-296**, their effect on gene transfer into primitive repopulating hematopoietic cells may also prove beneficial.

2/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09946196 99214334
Simultaneous infection with retroviruses pseudotyped with different envelope proteins bypasses viral receptor interference associated with colocalization of gp70 and target cells on fibronectin **CH-296**.
MacNeill EC; Hanenberg H; Pollok KE; van der Loo JC; Bierhuizen MF; Wagemaker G; Williams DA
Section of Pediatric Hematology/Oncology, Herman B Wells Center for Pediatric Research, Riley Hospital for Children, Indiana University School of Medicine, Indianapolis, Indiana, USA.
J Virol (UNITED STATES) May 1999, 73 (5) p3960-7, ISSN 0022-538X
Journal Code: KCV
Contract/Grant No.: P50DK49218, DK, NIDDK; PO1HL53586, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Several factors are thought to limit the efficiency of retroviral transduction in clinical gene therapy protocols that target hematopoietic stem cells. For example, the level of expression of the amphotropic receptor Pit-2, a phosphate symporter, appears to be low in human and murine hematopoietic stem cells. We have previously demonstrated that transduction of hematopoietic cells in the presence of the fibronectin (FN) fragment **CH-296** is extremely efficient (H. Hanenberg, X. L. Xiao, D. Dilloo, K. Hashino, I. Kato, and D. A. Williams, Nat. Med. 2:876-882, 1996). To examine functionally whether the retrovirus receptor is a limiting factor in transduction of hematopoietic cells, we performed competition experiments in the presence of FN **CH-296** with retrovirus vectors pseudotyped with the same or a different envelope protein. We demonstrate in both human erythroleukemia (HEL) cells and primary human CD34(+) hematopoietic cells inhibition of efficient infection due to receptor interference when two vectors targeting the amphotropic receptor are used simultaneously. Receptor interference lasted up to 24 h. No interference was demonstrated when vectors targeting the amphotropic receptor and the gibbon ape leukemia virus (GALV) receptor Pit-1 were used concurrently. In contrast, simultaneous infection with vectors targeting both Pit-1 and Pit-2 yielded transduction efficiencies consistently higher than with either vector alone in both HEL cells and human CD34(+) hematopoietic cells. These data demonstrate that the use of FN **CH-296** leads to amphotropic receptor saturation in these cells. Simultaneous infection with vectors targeting both amphotropic and GALV receptors may prove to be of additional benefit in the design of gene therapy protocols.

2/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09779499 99055517
Highly efficient transduction of the green fluorescent protein gene in human umbilical cord blood stem cells capable of cobblestone formation in long-term cultures and multilineage engraftment of immunodeficient mice.
van Hennik PB; Verstegen MM; Bierhuizen MF; Limon A; Wognum AW; Cancelas JA; Barquinero J; Ploemacher RE; Wagemaker G

Institute of Hematology, Erasmus University Rotterdam, The Netherlands; and the Department of Cryobiology and Cell Therapy, Institut de Recerca Oncologica, Barcelona, [redacted]in.

Blood (UNITED STATES) Dec 1 1998, 92 (11) p4013-22, ISSN 0006-4971 Journal Code: A8G

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Purified CD34(+) and CD34(+)CD38(-) human umbilical cord blood (UCB) cells were transduced with the recombinant variant of Moloney murine leukemia virus (MoMLV) MFG-EGFP or with SF-EGFP, in which EGFP expression is driven by a hybrid promoter of the spleen focus-forming virus (SFFV) and the murine embryonic stem cell virus (MESV). Infectious MFG-EGFP virus was produced by an amphotropic virus producer cell line (GP+envAm12). SF-EGFP was produced in the PG13 cell line pseudotyped for the gibbon ape leukemia virus (GaLV) envelope proteins. Using a 2-day growth factor prestimulation, followed by a 2-day, fibronectin fragment **CH-296**-supported transduction, CD34(+) and CD34(+)CD38(-) UCB subsets were efficiently transduced using either vector. The use of the SF-EGFP/PG13 retroviral packaging cell combination consistently resulted in twofold higher levels of EGFP-expressing cells than the MFG-EGFP/Am12 combination. Transplantation of 10(5) input equivalent transduced CD34(+) or 5 x 10(3) input equivalent CD34(+)CD38(-) UCB cells in nonobese diabetic/severe combined immunodeficient (NOD/SCID) mice resulted in median engraftment percentages of 8% and 5%, respectively, which showed that the in vivo repopulating ability of the cells had been retained. In addition, mice engrafted after transplantation of transduced CD34(+) cells using the MFG-EGFP/Am12 or the SF-EGFP/PG13 combination expressed EGFP with median values of 2% and 23% of human CD45(+) cells, respectively, which showed that the NOD/SCID repopulating cells were successfully transduced. EGFP+ cells were found in all human hematopoietic lineages produced in NOD/SCID mice including human progenitors with in vitro clonogenic ability. EGFP-expressing cells were also detected in the human cobblestone area-forming cell (CAFC) assay at 2 to 6 weeks of culture on the murine stromal cell line FBMD-1. During the transduction procedure the absolute numbers of CAFC week 6 increased 5- to 10-fold. The transduction efficiency of this progenitor cell subset was similar to the fraction of EGFP+ human cells in the bone marrow of the NOD/SCID mice transplanted with MFG-EGFP/Am12 or SF-EGFP/PG13 transduced CD34(+) cells, ie, 6% and 27%, respectively. The study thus shows that purified CD34(+) and highly purified CD34(+)CD38(-) UCB cells can be transduced efficiently with preservation of repopulating ability. The SF-EGFP/PG13 vector/packaging cell combination was much more effective in transducing repopulating cells than the MFG-EGFP/Am12 combination.

2/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09743653 99025925

Gene delivery to human B-precursor acute lymphoblastic leukemia cells.

Mascarenhas L; Stripecke R; Case SS; Xu D; Weinberg KI; Kohn DB

Divisions of Research Immunology/Bone Marrow Transplantation and Hematology/ Oncology, Department of Pediatrics, University of Southern California School of Medicine, Childrens Hospital Los Angeles, Los Angeles, CA, USA.

Blood (UNITED STATES) Nov 15 1998, 92 (10) p3537-45, ISSN 0006-4971 Journal Code: A8G

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Autologous leukemia cells engineered to express immune-stimulating molecules may be used to elicit antileukemia immune responses. Gene delivery to human B-precursor acute lymphoblastic leukemia (ALL) cells was investigated using the enhanced green fluorescent protein (EGFP) as a reporter gene, measured by flow cytometry. Transfection of the Nalm-6 and

Reh B-precursor ALL leukemia cell lines with an expression plasmid was investigated using lipofection, electroporation, and a polycationic compound. Only the liposomal compound Cellfectin showed significant gene transfer (3.9% to 12% for Nalm-6 cells and 3.1% to 5% for Reh cells). Transduction with gibbon-ape leukemia virus pseudotyped Moloney murine leukemia virus (MoMuLV)-based retrovirus vectors was investigated in various settings. Cocultivation of ALL cell lines with packaging cell lines showed the highest transduction efficiency for retroviral gene transfer (40.1% to 87.5% for Nalm-6 cells and 0.3% to 9% for Reh cells), followed by transduction with viral supernatant on the recombinant fibronectin fragment **CH-296** (13% to 35.5% for Nalm-6 cells and 0.4% to 6% Reh cells), transduction on human bone marrow stroma monolayers (3.2% to 13.3% for Nalm-6 cells and 0% to 0.2% Reh cells), and in suspension with protamine sulfate (0.7% to 3.1% for Nalm-6 cells and 0% for Reh cells). Transduction of both Nalm-6 and Reh cells with human immunodeficiency virus-type 1 (HIV-1)-based lentiviral vectors pseudotyped with the vesicular stomatitis virus-G envelope produced the best gene transfer efficiency, transducing greater than 90% of both cell lines. Gene delivery into primary human B-precursor ALL cells from patients was then investigated using MoMuLV-based retrovirus vectors and HIV-1-based lentivirus vectors. Both vectors transduced the primary B-precursor ALL cells with high efficiencies. These studies may be applied for investigating gene delivery into primary human B-precursor ALL cells to be used for immunotherapy.

2/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09652231 98395178

VLA-5 is expressed by mouse and human long-term repopulating hematopoietic cells and mediates adhesion to extracellular matrix protein fibronectin.

van der Loo JC; Xiao X; McMillin D; Hashino K; Kato I; Williams DA

Department of Pediatrics, Section of Hematology/Oncology, Herman B Wells Center for Pediatric Research, James Whitcomb Riley Hospital for Children, Indiana University School of Medicine, Indianapolis, Indiana 46202, USA.

J Clin Invest (UNITED STATES) Sep 1 1998, 102 (5) p1051-61, ISSN 0021-9738 Journal Code: HS7

Contract/Grant No.: P50 DK 49218, DK, NIDDK

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Fibronectin (FN), an extracellular matrix protein, is involved in the adhesion and migration of hematopoietic cells and has been shown to enhance retroviral gene transfer into primitive hematopoietic cells by co-localization of target cells and retrovirus when used as a substrate in vitro. We have previously found that mouse hematopoietic stem cells could be transduced on a FN fragment that included the recognition sequence Arg-Gly-Asp (RGD), suggesting that stem cells may express the integrin very late antigen (VLA)-5. To address this, we investigated the binding of mouse and human hematopoietic cells to recombinant peptides that contained one or a combination of the three principle cell-binding domains of FN. These domains included the VLA-5- binding sequence RGD, the VLA-4-binding site CS1, and the high affinity heparin-binding domain. Here we show that mouse long-term in vivo repopulating stem cells, as well as primitive human NOD/SCID mouse repopulating cells, can bind extracellular matrix protein FN by using integrin VLA-5 in vitro. This binding is specific and can be inhibited by antibodies to VLA-5. In addition, preincubation of BM cells with peptide **CH-296** , which contains all three primary FN-binding domains, decreased the engraftment of cells in the bone marrow in vivo, while intravenous injection of the same peptide induced an increase of progenitor cells in the spleen. In summary, our data demonstrate that VLA-5 is expressed on primitive mouse and human hematopoietic cells and suggest that there may be significant cooperation

between integrin receptors and proteoglycan molecules in the engraftment of bone marrow cells and hematopoietic cell adhesion in vivo.

2/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09648925 98402333
Improved gene transfer into baboon marrow repopulating cells using recombinant human fibronectin fragment **CH-296** in combination with interleukin-6, stem cell factor, FLT-3 ligand, and megakaryocyte growth and development factor.
Kiem HP; Andrews RG; Morris J; Peterson L; Heyward S; Allen JM; Rasko JE; Potter J; Miller AD
Clinical Research and Molecular Medicine Divisions, Fred Hutchinson Cancer Research Center, Seattle, WA, USA. hkiem@fhcrc.org
Blood (UNITED STATES) Sep 15 1998, 92 (6) p1878-86, ISSN 0006-4971 Journal Code: A8G
Contract/Grant No.: P50 HL54881, HL, NHLBI; P30 CA15704, CA, NCI; N01 AI35191, AI, NIAID; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have used a competitive repopulation assay in baboons to develop improved methods for hematopoietic stem cell transduction and have previously shown increased gene transfer into baboon marrow repopulating cells using a gibbon ape leukemia virus (GALV)-pseudotype retroviral vector (Kiem et al, Blood 90:4638, 1997). In this study using GALV-pseudotype vectors, we examined additional variables that have been reported to increase gene transfer into hematopoietic progenitor cells in culture for their ability to increase gene transfer into baboon hematopoietic repopulating cells. Baboon marrow was harvested after in vivo administration (priming) of stem cell factor (SCF) and granulocyte colony-stimulating factor (G-CSF). CD34-enriched marrow cells were divided into two equal fractions to directly compare transduction efficiencies under different gene transfer conditions. Transduction by either incubation with retroviral vectors on **CH-296** -coated flasks or by cocultivation on vector-producing cells was studied in five animals; in one animal, transduction on **CH-296** was compared with transduction on bovine serum albumin (BSA)-coated flasks. The highest level of gene transfer was obtained after 24 hours of prestimulation followed by 48 hours of incubation on **CH-296** in vector-containing medium in the presence of multiple hematopoietic growth factors (interleukin-6, stem cell factor, FLT-3 ligand, and megakaryocyte growth and development factor). Using these conditions, up to 20% of peripheral blood and marrow cells contained vector sequences for more than 20 weeks, as determined by both polymerase chain reaction and Southern blot analysis. Gene transfer rates were higher for cells transduced on **CH-296** as compared with BSA or cocultivation. In one animal, we have used a vector expressing a cell surface protein (human placental alkaline phosphatase) and have detected 10% and 5% of peripheral blood cells expressing the transduced gene 2 and 4 weeks after transplantation as measured by flow cytometry. In conclusion, the conditions described here have resulted in gene transfer rates that will allow detection of transduced cells by flow cytometry to facilitate the evaluation of gene expression. The levels of gene transfer obtained with these conditions suggest the potential for therapeutic efficacy in diseases affecting the hematopoietic system. Copyright 1998 by The American Society of Hematology.

2/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09597016 98269032

Enhancement of retroviral gene transduction on a dish coated with a cocktail of two different polypeptides: one exhibiting binding activity toward target cells, and the other toward retroviral vectors.

Asada K; Uemori T; Ueno T; Hashino K; Koyama N; Kawamura A; Kato I

Biotechnology Research Laboratories, Takara Shuzo Co., Ltd., Otsu, Shiga 520-2193, Japan.

J Biochem (Tokyo) (JAPAN) Jun 1998, 123 (6) p1041-7, ISSN 0021-924X
Journal Code: HIF

Languages: ENGLISH

Document type: JOURNAL ARTICLE

CH-296 , a recombinant fragment of human fibronectin (FN) composed of the cell-binding domain (C-domain), heparin-binding domain II (H-domain), and CS1 site, enhances the retrovirus-mediated gene transduction (GT) of hematopoietic stem cells. The RGD sequence in the C-domain is recognized by a variety of cell types through integrin VLA-5, and the LDV sequence in the CS1-site is recognized by integrin VLA-4. Retrovirus particles were also found to bind to the H-domain. Consequently, the **CH-296** fragment can enhance GT through binding to both retrovirus particles and target cells that express integrins VLA-5 and/or VLA-4. In this study, we found that the GT efficiency can be maintained at levels comparable to that of CH-271, a FN fragment similar to **CH-296** but lacking the CS1 site, when a cocktail of separated functional domains of CH-271 is used. When a dish was coated with a mixture of the C-domain and H-domain (molar ratio, 1:10), the GT efficiency of NIH3T3 cells reached the same level as that of the mother fragment, CH-271. The H-domain in the cocktail can be replaced with other virus-binding components, polylysine, FGF, and the insulin-binding domain of ColV, without the loss of GT efficiency. With other than FN fragments, a cocktail of erythropoietin and polylysine caused higher GT efficiency of Epo-receptor expressing TF-1 cells than in the case of each component alone.

2/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09545049 98301296

Stroma-conditioned medium and sufficient prestimulation improve fibronectin fragment-mediated retroviral gene transfer into human primitive mobilized peripheral blood stem cells through effects on their recovery and transduction efficiency.

Breems DA; Van Driel EM; Hawley RG; Siebel KE; Ploemacher RE

Institute of Hematology, Erasmus University Rotterdam, The Netherlands.

Leukemia (ENGLAND) Jun 1998, 12 (6) p951-9, ISSN 0887-6924
Journal Code: LEU

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Mobilized peripheral blood stem cells (PBSC) are an attractive vehicle for cancer gene therapy. However these stem cells may have a reduced proliferative capacity due to previous cytotoxic chemotherapy treatment of the patient. In addition, primitive hematopoietic stem cells (HSC) from mobilized peripheral blood are almost exclusively quiescent, which makes it hard to induce proliferation in vitro and thus to improve stable transduction of introduced genes into a sufficiently large number of primitive stem cells. In this study CD34-selected mobilized PBSC from lymphoma and myeloma patients were used as target cells for retroviral-mediated gene transfer using a clinically relevant cell- and serum-free supernatant transduction protocol. We have investigated various parameters that may contribute to an improvement of the poor transduction efficiency of the primitive HSC, including prestimulation time, the use of the carboxy-terminal fibronectin fragment **CH-296**, as well as stromal cell line conditioned media. Retroviral supernatant transduction in combination with **CH-296** increased significantly the gene transfer efficiency as compared to supernatant alone and made the use of

polycations redundant. Gene transfer of primitive HSC (cobblestone area forming cell (CAFC) week 6) was specifically improved when this procedure was preceded by a 5-day pre-culture period as compared to a 2-day transduction procedure. However, irrespective of the numerical recovery, the CAFC week 6 after retroviral transduction produced less long-term culture colony-forming cells, suggesting a loss of individual stem cell quality. The addition of stroma-conditioned media during the pre-culture period did not affect the individual CAFC quality or transduction efficiency, but increased greatly the recovery of the total number of transduced and untransduced HSC leading to larger grafts containing higher numbers of transduced stem cells.

2/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09505595 98241726
High-efficiency gene transfer into normal and adenosine deaminase-deficient T lymphocytes is mediated by transduction on recombinant fibronectin fragments.
Pollok KE; Hanenberg H; Noblitt TW; Schroeder WL; Kato I; Emanuel D; Williams DA
Section of Pediatric Hematology/Oncology, Herman B. Wells Center for Pediatric Research, Riley Hospital for Children, Indiana University School of Medicine, Indianapolis, Indiana 46202-5525, USA.
J Virol (UNITED STATES) Jun 1998, 72 (6) p4882-92, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: PO1 HL 53586, HL, NHLBI; P50 DK 49218, DK, NIDDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Primary human T lymphocytes are powerful targets for genetic modification, although the use of these targets in human gene therapy protocols has been hampered by low levels of transduction. We have shown previously that significant increases in the transduction of hematopoietic stem and progenitor cells with retroviral vectors can be obtained by the colocalization of the retrovirus and target cells on specific fibronectin (FN) adhesion domains (H. Hanenberg, X. L. Xiao, D. Dilloo, K. Hashino, I. Kato, and D. A. Williams, Nat. Med. 2:876-882, 1996). We studied the transfer of genes into primary T lymphocytes by using FN-assisted retroviral gene transfer. Activated T lymphocytes were infected for three consecutive days on the recombinant FN fragment **CH-296** with a retroviral vector encoding the murine B7-1 protein. Transduced lymphocytes were analyzed for murine B7-1 expression, and it was found that under optimal conditions, 80 to 89% of the CD3+ lymphocytes were transduced. Gene transfer was predominantly augmented by the interaction between VLA-4 on the T lymphocytes and the FN adhesion site CS-1. Adenosine deaminase (ADA)-deficient primary T lymphocytes transduced on **CH-296** with a retrovirus encoding murine ADA (mADA) exhibited levels of mADA activity severalfold higher than the levels of the endogenous human ADA protein observed in normal human T lymphocytes. Strikingly, the long-term expression of the transgene was dependent on the activation status of the lymphocytes. This approach will have important applications in human gene therapy protocols targeting primary T lymphocytes.

2/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09424734 98139444
Retroviral-mediated gene transfer of the leukocyte integrin CD18 into peripheral blood CD34+ cells derived from a patient with leukocyte adhesion deficiency type 1.
Bauer TR; Schwartz BR; Conrad Liles W; Ochs HD; Hickstein DD

Medical Research Service, VA Puget Sound Health Care System, Seattle, WA 98108, USA.
Blood (UNITED STATES) Mar 1 1998, 91 (5) p1520-6, ISSN 0006-4971
Journal Code: A8G
Contract/Grant No.: DK48456, DK, NIDDK; HL54881, HL, NHLBI; HL53515, HL, NHLBI; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Leukocyte adhesion deficiency or LAD is a congenital immunodeficiency disease characterized by recurrent bacterial infections in which the leukocytes from affected children fail to adhere to endothelial cells and migrate to the site of infection due to heterogeneous defects in the leukocyte integrin CD18 subunit. To assess the feasibility of human gene therapy of LAD, we transduced granulocyte colony-stimulating factor (G-CSF)-mobilized, CD34+ peripheral blood stem cells derived from a patient with the severe form of LAD using supernatant from the retroviral vector PG13/LgCD18. The highest transduction frequencies (31%) were found after exposure of the cells to retroviral vector on a substrate of recombinant fibronectin fragment **CH-296** in the presence of growth factors interleukin-3 (IL-3), IL-6, and stem cell factor. When the phenotype of the transduced cells was monitored by fluorescence-activated cell sorting following in vitro differentiation with growth factors G-CSF and granulocyte-macrophage CSF (GM-CSF), CD11a surface expression was detected immediately after transduction. CD11b and CD11c were expressed at low levels immediately following transduction, but increased over 3 weeks in culture. Adhesion of the transduced cells was nearly double that of nontransduced cells in a cell adhesion assay using human umbilical vein endothelial cells. Transduced cells also demonstrated the ability to undergo a respiratory burst in response to opsonized zymosan, a CD11/CD18-dependent ligand. These experiments show that retrovirus-mediated gene transfer of the CD18 subunit complements the defect in LAD CD34+ cells resulting in CD11/CD18 surface expression, and that the differentiated myelomonocytic cells derived from the transduced LAD CD34+ cells display CD11/CD18-mediated adhesion function. These results indicate that ex vivo gene transfer of CD18 into LAD CD34+ cells, followed by re-infusion of the transduced cells, may represent a therapeutic approach to LAD.

2/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09401906 98109427
Optimization of fibronectin-assisted retroviral gene transfer into human CD34+ hematopoietic cells.
Hanenberg H; Hashino K; Konishi H; Hock RA; Kato I; Williams DA
Herman B Wells Center for Pediatric Research, Riley Hospital for Children, Indiana University School of Medicine, Indianapolis 46202-5225, USA.
Hum Gene Ther (UNITED STATES) Dec 10 1997, 8 (18) p2193-206, ISSN 1043-0342 Journal Code: A12
Contract/Grant No.: P01 HL 53586, HL, NHLBI; P50 DK 49218, DK, NIDDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Efficient retroviral gene transfer into hematopoietic stem and progenitor cells can be achieved by co-localizing retrovirus and target cells on specific adhesion domains of recombinant fibronectin (FN) fragments. In this paper, we further optimize this technology for human CD34+ cells. Investigating the role of cytokine prestimulation in retrovirus-mediated gene transfer on plates coated with the recombinant FN **CH-296** revealed that prestimulation of granulocyte colony-stimulating factor (G-CSF)-mobilized peripheral blood (PB) CD34+ cells was essential to achieve efficient gene transfer into clonogenic cells. The highest gene transfer occurred by prestimulating PB CD34+ cells for 40 hr with a combination of stem cell factor (SCF), G-CSF, and megakaryocyte growth and

development factor (MGDF) prior to retroviral infection on **CH-296**. Surprisingly, a prolonged simultaneous exposure of primary CD34+ PB cells to retrovirus and cytokines in the presence of **CH-296** lowered the gene transfer efficiency. Gene transfer into cytokine prestimulated CD34+ bone marrow (BM) cells was not influenced by increasing the coating concentrations of a recombinant FN fragment, **CH-296**, nor was it adversely influenced by increasing the number of CD34+ target cells, suggesting that the amount of retroviral particles present in the supernatant was not a limiting factor for transduction of CD34+ BM cells on **CH-296**-coated plates. The polycation Polybrene was not required for efficient transduction of hematopoietic cells in the presence of **CH-296**. Furthermore, we demonstrated that repeated exposure of **CH-296** to retrovirus containing supernatant, called preloading, can be employed to concentrate the amount of retroviral particles bound to **CH-296**. These findings establish a simple and short clinically applicable transduction protocol that targets up to 68% of BM or G-CSF-mobilized PB CD34+ cells and is capable of genetically modifying up to 17% of CD34+CD38-/dim PB cells.

2/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06862152 92105063
Production and characterization of functional domains of human fibronectin expressed in Escherichia coli.
Kimizuka F; Taguchi Y; Ohdate Y; Kawase Y; Shimojo T; Hashino K; Kato I; Sekiguchi K; Titani K
Biotechnology Research Laboratories, Takara Shuzo Co., Ltd., Shiga.
J Biochem (Tokyo) (JAPAN) Aug 1991, 110 (2) p284-91, ISSN 0021-924X
Journal Code: HIF
Languages: ENGLISH
Document type: JOURNAL ARTICLE
An efficient expression system was constructed in Escherichia coli that produced a 33-kDa fragment, C-274, of human fibronectin with a strong cell-adhesive activity. The entire sequence of the heparin-binding domain with 271 amino acids, H-271, was also expressed. Deletion analysis of the type III repeats showed that the heparin-binding site was at type III-13. The cell-adhesive activity of a fusion protein, CH-271, containing the cell- and the heparin-binding domains was twice that of C-274 when BHK but not B16-F10 melanoma cells were tested; H-271 alone was inactive. Recombinant proteins containing the CS1 sequence of the IIICS region were more active than C-274 and CH-271 with B16-F10. However, H-296, which contained both H-271 and CS1, was almost inactive with BHK. **CH-296**, which contained CS1 at the C-terminus of CH-271, was more active with B16-F10 than H-296 and C-CS1, which was produced by the deletion of H-271 from **CH-296**. Thus, the cell-binding domain was active with both kinds of cells. The heparin-binding domain promoted the adhesion of both kinds of cells only when linked to the cell-binding domain or CS1. CS1 was specific for the adhesion of B16-F10 but was not essential.

2/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06837841 92064541
Inhibitory effect of fibronectin and its recombinant polypeptides on the adhesion of metastatic melanoma cells to laminin.
Saiki I; Makabe T; Yoneda J; Murata J; Ishizaki Y; Kimizuka F; Kato I; Azuma I
Institute of Immunological Science, Hokkaido University, Sapporo.
Jpn J Cancer Res (JAPAN) Oct 1991, 82 (10) p1112-9, ISSN 0910-5050
Journal Code: HBA

Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have utilized recombinant fibronectin fragments with cell-binding domain (C-274), heparin-binding domain (H-271) or CS1 peptide in type III connecting segment (IIICS) and their fusion polypeptides such as **CH-296** (containing C-274, H-271 and CS1), CH-271 (containing C-274 and H-271) and C-CS1 (containing C-274 and CS1) to investigate the mechanism of the fibronectin-mediated inhibitory effect on tumor cell adhesion to laminin as well as fibronectin. These fragments retained cell adhesion-promoting and/or heparin-binding properties when they were immobilized on a surface. Pretreatment of tumor cells with **CH-296** or CH-271 suppressed cell adhesion to both laminin and fibronectin. H-271 at the high concentration of 500 micrograms/ml slightly inhibited cell adhesion to laminin (but not to fibronectin), whereas C-274, C-CS1 or a mixture of C-274, H-271 and CS1 (similar molar ratio to **CH-296**) inhibited cell adhesion to fibronectin but not to laminin. On the other hand, tumor cell adhesion to laminin-substrate was also inhibited by heparin or heparan sulfate, which were able to bind to laminin, suggesting that heparin-like molecules on the cell surface may be included among the laminin receptors. These results indicated that the co-presence of cell- and heparin-binding domains of fibronectin may be required for the fibronectin-mediated inhibitory effect on tumor cell adhesion to laminin, and that the interaction of the heparin-binding domain of fibronectin with the cell surface leads to the inhibition of the cell adhesion to laminin.

2/3,AB/20 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11867782 BIOSIS NO.: 199900113891
Enhanced gene transfer into CML and normal bone marrow, and CML and mobilised peripheral blood CD34+ cells, using the recombinant fibronectin fragment **CH-296**.
AUTHOR: Garrett E; Miller A R-M; Goldman J M; Melo J V; Apperley J F
AUTHOR ADDRESS: Dep. Haematol., Imperial Coll. Sch. Med., Hammersmith Hosp., Du Cane Road, London W12 0NN**UK
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p377B Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/21 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11862340 BIOSIS NO.: 199900108449
The use of cytokines active on primitive hematopoietic cells and stromal or fibronectin support during transduction improves stable retroviral gene transfer into primate CD34+ hematopoietic cells to clinically relevant levels.
AUTHOR: Wu T(a); Sellers S E; Kim H J; Agricola B A; Metzger M E; Donahue R E; Dunbar C E; Tisdale J F
AUTHOR ADDRESS: (a)Hematol. Branch, NHLBI, NIH, Bethesda, MD**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p689A Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/22 (Item 3 [redacted]om file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11862247 BIOSIS NO.: 199900108356
Thrombopoietin combined with FLT3 and KIT ligands increases the transduction efficiency of human primitive hematopoietic progenitors, and novel 'SAR' retroviral vectors allow maintenance of NGFR transgene expression in vivo.
AUTHOR: Murray L J; Luens K M; Travis M A; Tushinski R J; Plavec I; Forestell S; Hansteen G; Chen J; Young J C; Hill B L
AUTHOR ADDRESS: SyStemix Inc., A Novartis Co., Palo Alto, CA**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p466A-467A Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/23 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11862246 BIOSIS NO.: 199900108355
Increased transduction into early human cord blood progenitor cells by centrifugation enhanced transduction in fibronectin fragment coated tubes.
AUTHOR: Sanyal A; Kawamura M; Zaboikin M; Mineishi S; Schuening F G
AUTHOR ADDRESS: Bone Marrow Transplant Div., Univ. Wis., Madison, WI 53792 **USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p466A Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/24 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11856126 BIOSIS NO.: 199900102235
Extended production of oxidase normal neutrophils in X-linked chronic granulomatous disease (CGD) following gene therapy with gp91phox transduced CD34+ cells.
AUTHOR: Malech H L(a); Horwitz M E; Linton G F; Theobald-Whiting N; Brown M R; Farrell C J; Butz R E; Carter C S; Decarlo E; Miller J A; Van Epps D E ; Read E J; Fleisher T A
AUTHOR ADDRESS: (a)Lab. Host Defenses, Natl. Inst. Allergy Infect. Dis., Natl. Inst. Health, Bethesda, MD**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p690A Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/25 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2000 BIOSIS. All rights reserv.

11852580 BIOSIS NO.: 199900098689
Relationship of target cell adhesion, viral adhesion, and retroviral transduction efficiency in fibronectin fragment **CH-296**, human stroma, and stromal cell lines.
AUTHOR: Kawamura M; Zaboikin M; Anderson C; Jarecki H; Sanyal A; Schuening F; Mineishi S
AUTHOR ADDRESS: Bone Marrow Transplant Div., Univ. Wis., Madison, WI**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p469A Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/26 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2000 BIOSIS. All rts. reserv.

11851911 BIOSIS NO.: 199900098020
Gene transfer into canine hematopoietic repopulating cells.
AUTHOR: Goerner M; Buron G; Storb R; Kiem H-P
AUTHOR ADDRESS: Fred Hutchinson Cancer Res. Cent., Univ. Washington, Seattle, WA**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p688A-689A Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/27 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2000 BIOSIS. All rts. reserv.

11851873 BIOSIS NO.: 199900097982
Delineation of molecular mechanisms regulating transgene expression in human T lymphocytes and hematopoietic CD34+ cells transduced at high efficiency with Moloney murine leukemia viruses.
AUTHOR: Pollok Karen E(a); Van Der Loo Johannes C M; Williams David A
AUTHOR ADDRESS: (a)Sect. Pediatr. Hematol. and Oncol., Herman B. Wells Cent. Pediatr. Res., Riley Hosp. Child., Ind**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p466A Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/28 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2000 BIOSIS. All rts. reserv.

11849308 BIOSIS NO.: 199900095417
Highly efficient MDR-1 gene transfer into humans using mobilized CD34+ cells transduced over recombinant fibronectin **CH-296**

fragment.
AUTHOR: Abonour R(a); Einhorn L; Hromas R; Robertson M J; Srout E; Traycoff C M; Bank A; Kato I; [redacted]ada K; Croop J; Smith F O; Wil[redacted]ms D A; Cornetta K
AUTHOR ADDRESS: (a)Indiana Cancer Res. Cent., Indiana Univ. Sch. Med., Indianapolis, IN**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p690A Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/29 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11286016 BIOSIS NO.: 199800067348
Gene transfer into baboon hematopoietic repopulating cells using recombinant human fibronectin fragment **CH-296**.
AUTHOR: Kiem H-P(a); Morris J; Heyward S; Peterson L; Potter J; Miller A D; Andrews R G
AUTHOR ADDRESS: (a)Fred Hutchinson Cancer Res. Cent., Seattle, WA**USA
JOURNAL: Blood 90 (10 SUPPL. 1 PART 1):p236A Nov. 15, 1997
CONFERENCE/MEETING: 39th Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997
SPONSOR: The American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/30 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10551901 BIOSIS NO.: 199699173046
High efficiency transduction of human CD34+ progenitors on fibronectin **CH 296** verified by clonal integration analysis.
AUTHOR: Dao M A(a); Hashino K; Kato I; Kohn D B; Williams D A; Nolta J A
AUTHOR ADDRESS: (a)Childrens Hosp. Los Angeles, Univ. Southern California Sch. Med., Los Angeles, CA**USA
JOURNAL: Experimental Hematology (Charlottesville) 24 (9):p1057 1996
CONFERENCE/MEETING: 25th Annual Meeting of the International Society for Experimental Hematology New York, New York, USA August 23-27, 1996
ISSN: 0301-472X
RECORD TYPE: Citation
LANGUAGE: English